

Appl. No. 10/634,645  
Response dated May 10, 2005  
Reply to Office Action of February 10, 2005

### **Amendments to the Claims**

This listing of claims will replace all prior version and listings of claims in the application:

### **Listing of Claims:**

1. (Currently amended): An isolated fusion protein comprising: (a) a membrane-translocating sequence comprising at least eight consecutive residues of SEQ ID NO: 1 (Ala-Ala-Val-Leu-Leu-Pro-Val-Leu-Leu-Ala-Ala-Pro), and (b) an I $\kappa$ B protein that has optimal permeability through a cell membrane.
2. (Original): The isolated fusion protein of claim 1, wherein the membrane-translocating sequence comprises at least nine consecutive residues of SEQ ID NO: 1.
3. (Original): The isolated fusion protein of claim 1, wherein the membrane-translocating sequence comprises at least ten consecutive residues of SEQ ID NO: 1.
4. (Original): The isolated fusion protein of claim 1, wherein the membrane-translocating sequence comprises at least eleven consecutive residues of SEQ ID NO: 1.
5. (Original): The isolated fusion protein of claim 1, wherein the membrane-translocating sequence comprises at least twelve consecutive residues of SEQ ID NO: 1.
6. (Original): The isolated fusion protein of claim 1, wherein the I $\kappa$ B protein protein comprises an I $\kappa$ B $\alpha$  protein.

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7. (Original): The isolated fusion protein of claim 1, wherein the I $\kappa$ B protein comprises an I $\kappa$ B $\beta$  protein.
8. (Original): The isolated fusion protein of claim 1, wherein the I $\kappa$ B protein comprises an I $\kappa$ B $\epsilon$  protein protein.
9. (Original): The isolated fusion protein of claim 1, wherein the I $\kappa$ B protein comprises a complex formed by two or more I $\kappa$ B proteins.
10. (Original): The isolated fusion protein of claim 1 further comprising a tag amino acid sequence or protein.
11. (Original): The isolated fusion protein of claim 10, wherein the tag amino acid sequence is selected from the group consisting of poly-arginine, poly-histidine, calmodulin-binding peptide (SEQ ID NO. 16), cellulose-binding domain, protein disulfide isomerase I (DsbA), c-myc (SEQ ID. NO. 12), glutathione S-transferase, a FLAG sequence (SEQ ID NO. 10), natural histidine tag (HAT; SEQ ID NO. 14), maltose-binding protein, transcript termination anti-termination factor (NusA), Staphylococcal protein A, Staphylococcal protein G, S--RNAase tag (SEQ ID NO. 13), streptavidin binding peptide (SEQ ID NO. 17), Strep-tag (SEQ ID. NO. 11), chitin-binding domain (SEQ ID NO. 18) and thioredoxin or any combination thereof.
12. (Original): The isolated fusion protein of claim 1 further comprising an antibody.
13. (Currently amended): A pharmaceutical composition comprising: (a) an isolated fusion protein having: (1) a membrane-translocating sequence comprising at least eight consecutive residues of SEQ ID NO: 1 (Ala-Ala-Val-Leu-Leu-Pro-Val-L- eu-Leu-Ala-

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Ala-Pro), and (2) an IκB protein that has optimal permeability through a cell membrane;  
and (b) a pharmaceutically acceptable carrier.

14. (Original): The pharmaceutical composition of claim 13, wherein the isolated fusion protein further comprises a tag amino acid sequence or protein.
15. (Original): The pharmaceutical composition of claim 14, wherein the tag amino acid sequence is selected from the group consisting of poly-arginine, poly-histidine, calmodulin-binding peptide (SEQ ID NO. 16), cellulose-binding domain, protein disulfide isomerase I (DsbA), c-myc (SEQ ID. NO. 12), glutathione S-transferase, a FLAG sequence (SEQ ID NO. 10), natural histidine tag (HAT; SEQ ID NO. 14), maltose-binding protein, transcript termination anti-termination factor (NusA), Staphylococcal protein A, Staphylococcal protein G, S-RNAase tag (SEQ ID NO. 13), streptavidin binding peptide (SEQ ID NO. 17), Strep-tag (SEQ ID. NO. 11), chitin-binding domain (SEQ ID NO. 18) and thioredoxin or any combination thereof.
16. (Original): The pharmaceutical composition of claim 13, wherein the isolated fusion protein further comprises an antibody.
17. (Withdrawn): A method for preventing an immune response in a host comprising administration of an isolated fusion protein, wherein the isolated fusion protein comprises: (a) a membrane-translocating sequence of about 8 to about 50 residues comprising at least eight consecutive residues of SEQ ID NO: 1 (Ala-Ala-Val-Leu-Leu-Pro-Val-Leu-Leu-Ala-Ala-Pro), and (b) an IκB protein.
18. (Withdrawn): The method of claim 17, wherein the membrane-translocating sequence comprises at least nine consecutive residues of SEQ ID NO: 1.

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19. (Withdrawn): The method of claim 17, wherein the membrane-translocating sequence comprises at least ten consecutive residues of SEQ ID NO: 1.
20. (Withdrawn): The method of claim 17, wherein the membrane-translocating sequence comprises at least eleven consecutive residues of SEQ ID NO: 1.
21. (Withdrawn): The method of claim 17 wherein the membrane-translocating sequence comprises at least twelve consecutive residues of SEQ ID NO: 1.
22. (Withdrawn): The method of claim 17, wherein the I $\kappa$ B protein comprises an I $\kappa$ B $\alpha$  protein.
23. (Withdrawn): The method of claim 17, wherein the I $\kappa$ B protein comprises an I $\kappa$ B $\beta$  protein.
24. (Withdrawn): The method of claim 17, wherein the I $\kappa$ B protein comprises an I $\kappa$ B $\epsilon$  protein.
25. (Withdrawn): The method of claim 17, wherein the I $\kappa$ B protein comprises a complex formed by two or more I $\kappa$ B proteins.
26. (Withdrawn): The method of claim 17, wherein the isolated fusion protein further comprises a tag amino acid sequence or protein.
27. (Withdrawn): The method of claim 26, wherein the tag amino acid sequence is selected from the group consisting of poly-arginine, poly-histidine, calmodulin-binding peptide (SEQ ID NO. 16), cellulose-binding domain, protein disulfide isomerase I (DsbA), c-myc (SEQ ID. NO. 12), glutathione S-transferase, a FLAG sequence (SEQ ID NO. 10),

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natural histidine tag (HAT; SEQ ID NO. 14), maltose-binding protein, transcript termination anti-termination factor (NusA), Staphylococcal protein A, Staphylococcal protein G, S-RNAase tag (SEQ ID NO. 13), streptavidin binding peptide (SEQ ID NO. 17), Strep-tag (SEQ ID. NO. 11), chitin-binding domain (SEQ ID NO. 18) and thioredoxin or any combination thereof.

28. (Withdrawn): The method of claim 17, wherein the isolated fusion protein further comprises an antibody.
29. (Withdrawn): The method of claim 17, wherein the immune response is associated with at least one of an allergy, asthma, contact dermatitis, delayed-type hypersensitivity, a wound-healing, allergic rhinitis, food hypersensitivity, ectopic dermatitis, inflammatory bowel disease, an immunologic disease of the lung, eosinophilic pneumonias, idiopathic pulmonary fibrosis, hypersensitivity pneumonitis, an autoimmune or immune-mediated skin disease, a bullous skin disease, erythema multiforme, psoriasis, gluten-sensitive enteropathy, Whipple's disease, systemic lupus erythematis, rheumatoid arthritis, osteoarthritis, juvenile chronic arthritis, ankylosing spondylitis, systemic sclerosis, an idiopathic inflammatory myopathy, Sjogren's disease, pleuritis, sarcoidosis, amyloidosis, autoimmune hemolytic anemia, autoimmune thrombocytopenia, thyroiditis, diabetes mellitus, immune-mediated renal disease, myasthenia gravis, a demyelinating disease of the central or peripheral nervous system, idiopathic demyelinating polyneuropathy, Guillain-Barre syndrome, a chronic inflammatory demyelinating polyneuropathy, a hepatobiliary disease, an infectious or autoimmune chronic active hepatitis, primary biliary cirrhosis, granulomatous hepatitis, sclerosing cholangitis, Graves disease, a transplantation-associated disease, a graft rejection, and graft-versus-host disease.
30. (Withdrawn): The method of claim 17, wherein the immune response is caused by exposure to *Mycoplasma tuberculosis*.

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31. (Withdrawn): The method of claim 17, wherein the isolated fusion protein is administered prophylactically.
32. (Withdrawn): The method of claim 17, wherein the isolated fusion protein is administered therapeutically.
33. (Withdrawn): The method of claim 17, wherein the isolated fusion protein is administered by one or more of the following routes selected from the group consisting of intravenous, intradermal, subcutaneous, oral, inhalation, deep lung inhalation, transdermal, transmucosal, vaginal and rectal administration.
34. (Withdrawn): The method of claim 17, wherein the isolated fusion protein is administered as a liposome.
35. (Withdrawn): The method of claim 17, wherein the isolated fusion protein is administered as an aerosol.
36. (Withdrawn): The method of claim 17, wherein the infusion protein is administered in combination with a compound used to treat or prevent any immune-related disorder.
37. (Withdrawn): The method of claim 36, wherein the compound is an anti-inflammatory agent.
38. (Withdrawn): The method of claim 37, wherein the anti-inflammatory agent is selected from the group consisting of aspirin, diflunisal, mesalamine, salicylsalicylic acid, sodium thiosalicylate, choline salicylate, magnesium salicylate, olsalazine, sulfasalazine, indomethacin, suldinac, etodolac, mefenamate, meclofenamate, flufenamate, tolfenamate,

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etofenamate, tolmetin, ketorolac, diclofenac, ibuprofen, naproxen, fenoprofen, ketoprofen, flurbiprofen, oxaprozin, piroxicam, meloxicam, nabumetone, apazone, nimesulide, zileuton, gold salts, colchicine, allopurinol, beclomethasone, budesonide, flunisolide, triamcinolone, prednisone, cromolyn, nedocromil, albuterol, bitolterol, pirbuterol, salmeterol, terbutaline, theophylline and other methylxanthines, metaproterenol, systemic glucocorticoids, antibiotics, antiparasitic agents, antiprotozoal agents, antimalarial agents, isoniazid, rifampin, ethambutol, antifungal agents, antiviral agents, alkylating agent, an antimetabolites, retinal, tretinoin, isotretinoin, etretinate, acitretin, arotinoid, .beta.-carotene, calcipotriene, anthralin, psoralen, 5-methoxypsoralen, trioxsalen, coal tar, masoprocol, and any pharmaceutically acceptable prodrug or derivative thereof.

39. (Withdrawn): The method of claim 36, wherein the compound is an immunosuppressive agent or procedure.
40. (Withdrawn): The method of claim 39, wherein the immunosuppressive agent or procedure is selected form the group consisting of cyclosporine, tacrolimus, azathioprine, mycophenolate, methotrexate, an immunoglobulin, a monoclonal antibody, an Rh(D) immune globulin, methoxsalen, thalidomide, radiation, or any pharmaceutically acceptable prodrug or derivative thereof.
41. (Withdrawn): The method of claim 36, wherein the compound is an antihistamine agent.
42. (Withdrawn): The method of claim 41, wherein the antihistamine agent is selected from the group consisting of carbinoxamine, clemastine, diphenhydramine, dimenhydrinate, pyrilamine, tripeleminamine, chlorpheniramine, brompheniramine, hydrazine, cyclizine, meclizine, promethazine, acrivastine, cetirizine, astemizole, levocabastine, loratadine and terfenadine, or any pharmaceutically acceptable prodrug or derivative thereof.

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43. (Withdrawn): A method for treating an immune-related disorder in a host comprising administration of an isolated fusion protein, wherein the isolated fusion protein comprises: (a) a membrane-translocating sequence comprising at least eight consecutive residues of SEQ ID NO: 1 (Ala-Ala-Val-Leu-Leu-Pro- -Val-Leu-Leu-Ala-Ala-Pro), and (b) an I $\kappa$ B protein.
44. (Withdrawn): The method of claim 43, wherein the membrane-translocating sequence comprises at least nine consecutive residues of SEQ ID NO: 1.
45. (Withdrawn): The method of claim 43, wherein the membrane-translocating sequence comprises at least ten consecutive residues of SEQ ID NO: 1.
46. (Withdrawn): The method of claim 43, wherein the membrane-translocating sequence comprises at least eleven consecutive residues of SEQ ID NO: 1.
47. (Withdrawn): The method of claim 43, wherein the membrane-translocating sequence comprises at least twelve consecutive residues of SEQ ID NO: 1.
48. (Withdrawn): The method of claim 43, wherein the I $\kappa$ B protein comprises an I $\kappa$ B $\alpha$  protein.
49. (Withdrawn): The method of claim 43, wherein the I $\kappa$ B protein comprises an I $\kappa$ B $\beta$  protein.
50. (Withdrawn): The method of claim 43, wherein the I $\kappa$ B protein comprises an I $\kappa$ B $\epsilon$  protein.



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51. (Withdrawn): The method of claim 43, wherein the I $\kappa$ B protein comprises a complex formed by two or more I $\kappa$ B proteins.
52. (Withdrawn): The method of claim 43, wherein the isolated fusion protein further comprises a tag amino acid sequence or protein.
53. (Withdrawn): The method of claim 43, wherein the tag amino acid sequence is selected from the group consisting of poly-arginine, poly-histidine, calmodulin-binding peptide (SEQ ID NO. 16), cellulose-binding domain, protein disulfide isomerase I (DsbA), c-myc (SEQ ID NO. 12), glutathione S-transferase, a FLAG sequence (SEQ ID NO. 10), natural histidine tag (HAT; SEQ ID NO. 14), maltose-binding protein, transcript termination anti-termination factor (NusA), Staphylococcal protein A, Staphylococcal protein G, S-RNAase tag (SEQ ID NO. 13), streptavidin binding peptide (SEQ ID NO. 17), Strep-tag (SEQ ID NO. 11), chitin-binding domain (SEQ ID NO. 18) and thioredoxin or any combination thereof.
54. (Withdrawn): The method of claim 43, wherein the isolated fusion protein further comprises an antibody.
55. (Withdrawn): The method of claim 43, wherein the immune response is associated with at least one of an allergy, asthma, contact dermatitis, delayed-type hypersensitivity, a wound-healing, allergic rhinitis, food hypersensitivity, ectopic dermatitis, inflammatory bowel disease, an immunologic disease of the lung, eosinophilic pneumonias, idiopathic pulmonary fibrosis, hypersensitivity pneumonitis, an autoimmune or immune-mediated skin disease, a bullous skin disease, erythema multiforme, psoriasis, gluten-sensitive enteropathy, Whipple's disease, systemic lupus erythematis, rheumatoid arthritis, osteoarthritis, juvenile chronic arthritis, ankylosing spondylitis, systemic sclerosis, an idiopathic inflammatory myopathy, Sjogren's disease, pleuritis, sarcoidosis, amyloidosis,

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autoimmune hemolytic anemia, autoimmune thrombocytopenia, thyroiditis, diabetes mellitus, immune-mediated renal disease, myasthenia gravis, a demylenating disease of the central or peripheral nervous system, idiopathic demylenating polyneuropathy, Guillain-Barre syndrome, a chonic inflammatory demyelinating polyneuropathy, a hepatobiliary disease, an infectious or autoimmune chronic active hepatitis, primary biliary cirrhosis, granulomatous hepatitis, sclerlosing cholangitis, Graves disease, a transplantation-associated disease, a graft rejection, and graft-versus-host disease.

56. (Withdrawn): The method of claim 43, wherein the inflammatory response is caused by exposure to *Mycoplasma tuberculosis*.
57. (Withdrawn): The method of claim 43, wherein the fusion protein is administered therapeutically.
58. (Withdrawn): The method of claim 43, wherein the fusion protein is administered prophylactically.
59. (Withdrawn): The method of claim 43, wherein the isolated fusion protein is administered by one or more of the following routes selected from the group consisting of intravenous, intradermal, subcutaneous, oral, inhalation, deep lung inhalation, transdermal, transmucosal, vaginal and rectal administration.
60. (Withdrawn): The method of claim 43, wherein the isolated fusion protein is administered as a liposome.
61. (Withdrawn): The method of claim 43, wherein the isolated fusion protein is administered as an aerosol.

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62. (Withdrawn): The method of claim 43, wherein the infusion protein is administered in combination with a compound used to treat or prevent any immune-related disorder.
63. (Withdrawn): The method of claim 62, wherein the compound is an anti-inflammatory agent.
64. (Withdrawn): The method of claim 63, wherein the anti-inflammatory agent is selected from the group consisting of aspirin, diflunisal, mesalamine, salicylsalicylic acid, sodium thiosalicylate, choline salicylate, magnesium salicylate, olsalazine, sulfasalazine, indomethacin, suldinac, etodolac, mefenamate, meclofenamate, flufenamate, tolfenamate, etofenamate, tolmetin, ketorolac, diclofenac, ibuprofen, naproxen, fenoprofen, ketoprofen, flurbiprofen, oxaprozin, piroxicam, meloxicam, nabumetone, apazone, nimesulide, zileuton, gold salts, colchicine, allopurinol, beclomethasone, budesonide, flunisolide, triamcinolone, prednisone, cromolyn, nedocromil, albuterol, bitolterol, pirbuterol, salmeterol, terbutaline, theophylline and other methylxanthines, metaproterenol, systemic glucocorticoids, antibiotics, antiparasitic agents, antiprotozoal agents, antimalarial agents, isoniazid, rifampin, ethambutol, antifungal agents, antiviral agents, alkylating agent, an antimetabolites, retinal, tretinoin, isotretinoin, etretinate, acitretin, arotinoid, .beta.-carotene, calcipotriene, anthralin, psoralen, 5-methoxypsoralen, trioxsalen, coal tar, masoprocol, and any pharmaceutically acceptable prodrug or derivative thereof.
65. (Withdrawn): The method of claim 62, wherein the compound is an immunosuppressive agent or procedure.
66. (Withdrawn): The method of claim 65, wherein the immunosuppressive agent or procedure is selected form the group consisting of cyclosporine, tacrolimus, azathioprine, mycophenolate, methotrexate, an immunoglobulin, a monoclonal antibody, an Rh(D)

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immune globulin, methoxsalen, thalidomide, radiation, or any pharmaceutically acceptable prodrug or derivative thereof.

67. (Withdrawn): The method of claim 62, wherein the compound is an antihistamine agent.
68. (Withdrawn): The method of claim 67, wherein the antihistamine agent is selected from the group consisting of carbinoxamine, clemastine, diphenhydramine, dimenhydrinate, pyrilamine, tripeleminamine, chlorpheniramine, brompheniramine, hydrazine, cyclizine, meclizine, promethazine, acrivastine, cetirizine, astemizole, levocabastine, loratadine and terfenadine, or any pharmaceutically acceptable prodrug or derivative thereof.
69. (Withdrawn): A method for treating or preventing an apoptosis-related disorder in a host comprising administration of an isolated fusion protein, wherein the isolated fusion protein comprises: (a) a membrane-translocating sequence comprising at least eight consecutive residues of SEQ ID NO: 1 (Ala-Ala-Val-Leu-Leu-Pro-Val-Leu-Leu-Ala-Ala-Pro), and (b) an I $\kappa$ B protein.
70. (Withdrawn): The method of claim 69, wherein the membrane-translocating sequence comprises at least nine consecutive residues of SEQ ID NO: 1
71. (Withdrawn): The method of claim 69, wherein the membrane-translocating sequence comprises at least ten consecutive residues of SEQ ID NO: 1.
72. (Withdrawn): The method of claim 69, wherein the membrane-translocating sequence comprises at least eleven consecutive residues of SEQ ID NO: 1.
73. (Withdrawn): The method of claim 69, wherein the membrane-translocating sequence comprises at least twelve consecutive residues of SEQ ID NO: 1.

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74. (Withdrawn): The method of claim 69, wherein the I $\kappa$ B protein comprises an I $\kappa$ B $\alpha$  protein.
75. (Withdrawn): The method of claim 69, wherein the I $\kappa$ B protein comprises an I $\kappa$ B $\beta$  protein.
76. (Withdrawn): The method of claim 69, wherein the I $\kappa$ B protein comprises an I $\kappa$ B $\epsilon$  protein.
77. (Withdrawn): The method of claim 69, wherein the I $\kappa$ B protein comprises a complex formed by two or more I $\kappa$ B proteins.
78. (Withdrawn): The method of claim 69, wherein the isolated fusion protein further comprises a tag amino acid sequence or protein.
79. (Withdrawn): The method of claim 78, wherein the tag amino acid sequence is selected from the group consisting of poly-arginine, poly-histidine, calmodulin-binding peptide (SEQ ID NO. 16), cellulose-binding domain, protein disulfide isomerase I (DsbA), c-myc (SEQ ID. NO. 12), glutathione S-transferase, a FLAG sequence (SEQ ID NO. 10), natural histidine tag (HAT; SEQ ID NO. 14), maltose-binding protein, transcript termination anti-termination factor (NusA), Staphylococcal protein A, Staphylococcal protein G, S-RNAase tag (SEQ ID NO. 13), streptavidin binding peptide (SEQ ID NO. 17), Strep-tag (SEQ ID. NO. 11), chitin-binding domain (SEQ ID NO. 18) and thioredoxin or any combination thereof.
80. (Withdrawn): The method of claim 69, wherein the isolated fusion protein further comprises an antibody.

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81. (Withdrawn): The method of claim 69, wherein the apoptosis-related disease is cancer.
82. (Withdrawn): The method of claim 69, wherein the fusion protein is administered therapeutically.
83. (Withdrawn): The method of claim 69, wherein the fusion protein is administered prophylactically.
84. (Withdrawn): The method of claim 69, wherein the isolated fusion protein is administered by one or more of the following routes selected from the group consisting of intravenous, intradermal, subcutaneous, oral, inhalation, deep lung inhalation, transdermal, transmucosal, vaginal and rectal administration.
85. (Withdrawn): The method of claim 69, wherein the isolated fusion protein is administered as a liposome.
86. (Withdrawn): The method of claim 69, wherein the isolated fusion protein is administered as an aerosol.
87. (Withdrawn): An animal model to test the effects of an isolated fusion protein on an inflammatory response comprising: (a) injecting an animal host with said fusion protein, wherein the animal host expresses a reporter gene whose expression is mediated by a NF- $\kappa$ B -dependent process such that inflammation may induce the production of the reporter gene product; (b) stimulating inflammation; (c) visualizing and quantifying the reporter gene product; and, (d) comparing the amount of reporter gene product quantified in an animal host injected with said fusion protein with that of a control animal.

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88. (Withdrawn): The animal model of claim 87, wherein the isolated fusion protein comprises: (a) a membrane-translocating sequence comprising at least eight consecutive residues of SEQ ID NO: 1 (Ala-Ala-Val-Leu-Leu-Pro-Val-L- eu-Leu-Ala-Ala-Pro), and (b) an IκB protein.